Muir-Torre Syndrome: A Case Report

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ABSTRACT

Muir-Torre syndrome is an autosomal dominant genodermatosis associated with sebaceous neoplasms and visceral malignancies. Characteristic sebaceous neoplasms include sebaceous adenoma, sebaceous carcinoma, sebaceoma, and keratoacanthoma with sebaceous differentiation. The most common visceral malignancies are colorectal and genitourinary tumors. Investigations into the molecular genetics of Muir-Torre Syndrome have revealed an association with germ-line mutations in hMSH2 and hMLH1 genes. The clinical and histological features of a patient with Muir-Torre syndrome who had two sebaceous adenomas, multiple basal cell carcinomas, and frontal bossing in association with colon cancer are presented in this report. (*J Clin Aesthetic Dermatol.* 2009;2(8):30–32.)

An 81-year-old male presented with an asymptomatic tan papule on his left jaw line. The patient stated that the lesion had been present for several months. The patient had a history of numerous basal cell carcinomas (BCC), actinic keratoses (AKs), and one prior biopsy-proven sebaceous adenoma. In addition to multiple skin cancers, the patient had a history of coronary artery bypass graft surgery and a partial colectomy for colon carcinoma. The patient was unable to provide a family history as he was adopted.

Physical examination of the patient's left jaw line revealed a 0.4cm tan-to-yellow papule on a markedly erythematous base. An incidental finding of frontal bossing was also noted (Figure 1). A shave biopsy showed numerous pyriform sebaceous lobules associated with an increased number of darker, immature sebocytes at their periphery. The lobules were oriented perpendicularly to the skin surface (Figures 2 and 3).

The patient's sebaceous adenomas and BCCs were excised, and he was treated with long-term fluorouracil 5% cream applied twice weekly to his face, chest, and back as prophylaxis for AKs and cutaneous malignancies. He had skin examinations every three months as well as annual screening for internal malignancy. The patient developed more than 20 nodular and superficial BCCs on his face and trunk during his lifetime, which were treated by excision or electrodessication and curettage. He did not, however, develop metastases from his colon carcinoma or any additional internal malignancies. The patient died at age 87 of causes unrelated to his skin or colon carcinomas.

DISCUSSION

Muir-Torre syndrome (MTS) is a genodermatosis characterized by the presence of at least one sebaceous gland neoplasm and at least one visceral malignancy.[1–4] This rare disorder was first described by Muir et al in 1967 and Torre in 1968.[5,6] It has an autosomal dominant inheritance pattern with variable expression, though sporadic cases have been reported.[1,2] Germ-line mutations in hMSH2 and hMLH1 genes are often associated with this disorder, but are not required for diagnosis.[1,2,7,8] Mutations in the hMSH2 and hMLH1 lead to microsatellite instability within DNA, resulting in alteration or inactivation of tumor suppressor genes. MTS is thought to be a subset of nonpolyposis colorectal cancer since approximately 30 to 70 percent of patients with a clinical diagnosis of hereditary nonpolyposis colorectal cancer have a germ-line mutation in one of the mismatch repair genes, most commonly hMSH2 and hMLH1.[4,9]

Individuals with MTS may present with one visceral malignancy or develop multiple primary malignancies at different sites.[10] The most common visceral malignancies associated with MTS are colorectal followed by genitourinary.[2,4] Colon carcinoma most often occurs proximal to the splenic flexure in contrast to more distal locations in individuals who develop non-MTS colon carcinoma.[2,11] Less common malignancies include breast carcinoma, hematological disorders, endometrial carcinoma, and rarely gastric carcinoma.[1,3]

Sebaceous neoplasms have the potential to arise from any sebaceous gland in the body. They have the greatest predilection for the nose, eyelids, and other areas with

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abundant sebaceous glands.[12] Characteristic sebaceous gland neoplasms include sebaceous adenoma, sebaceous carcinoma, sebaceoma (sebaceous epitheliomas), and keratoacanthoma (KA) with sebaceous differentiation.[1,7] BCCs of any subtype can be associated with MTS. Most lesions occur in the head and neck region, while a small proportion involve the eyelid.[1] The occurrence of sebaceous neoplasms in the general population is rare. Thus, finding one of these tumors may represent a marker for MTS and should prompt a screening for visceral malignancy.[10] MTS occurs more frequently in males with a male-to-female ratio of 3:2.[2] The most common clinical presentation of lesions is a painless, pink-to-yellowish, round papule or subcutaneous nodule.[4,7] Some lesions are umbilicated resembling molluscum contagiosum.[4] It is important to note that while sebaceous hyperplasia can occur in these patients, it has not been associated with a diagnosis of MTS. However, sebaceous hyperplasia lesions with unusual features warrant further investigation.[1]

Histopathological evaluation of sebaceous adenomas reveal sebaceous lobules with a peripheral germinative layer of small basaloid cells that transition to mature sebaceous cells centrally. Sebaceous epitheliomas differ from sebaceous adenomas in that peripherally located basaloid cells outnumber the mature sebaceous component. Sebaceous carcinomas demonstrate malignant basaloid architecture with cytologic atypia, scattered mitoses, and variable sebaceous differentiation.[4]

While a diagnosis of MTS can be made with the presence of at least one sebaceous neoplasm associated with at least one primary visceral malignancy, multiple KAs and visceral malignancies occurring in the setting of a positive family history also fulfill diagnostic criteria.[1,4] Cystic sebaceous neoplasms have thus far only been observed in patients with MTS, so patients who have these lesions must undergo further testing.[2,4] Immunohistochemical staining for hMSH2 and hMLH1 can confirm a diagnosis of MTS after clinical criteria have been met.[1,2]

With the exception of sebaceous carcinomas, sebaceous neoplasms associated with MTS are typically of low malignant potential. They have almost no metastatic potential and therefore can be treated with complete excision. Sebaceous carcinomas, most commonly occurring in the periocular region, have been reported to metastasize in some cases. They are fairly aggressive with the tendency for angiolymphatic invasion and subsequent metastatic disease.[2,7] Frequency of metastasis and mortality has been reported to be as high as 25 percent in some studies.[7] Treatment with wide surgical excision or Mohs micrographic surgery is recommended for these lesions to significantly reduce recurrence in extraocular locations.[1,7] While topical 5-fluorouracil and imiquimod have been shown to prevent the AKs, KAs, and BCCs associated with this syndrome, chemoprophylaxis with oral isotretinoin alone or in combination with interferon alpha has been shown to suppress the development of sebaceous neoplasms in MTS.[4]

The presence of a sebaceous neoplasm may serve as the

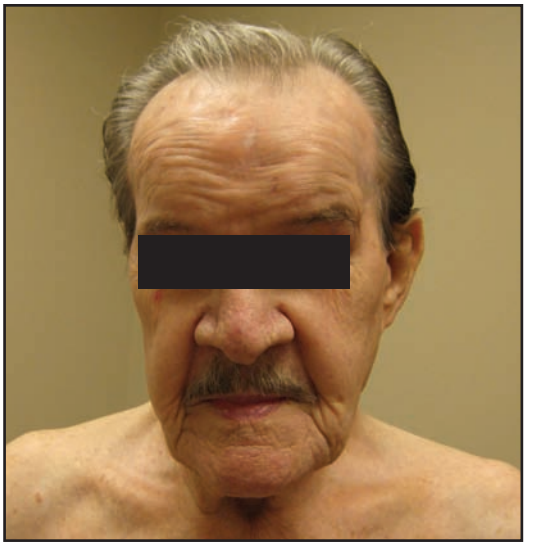

FIGURE 1. Patient at presentation. An incidental finding of an unusually prominent forehead and heavier-than-normal brow ridge known as frontal bossing.

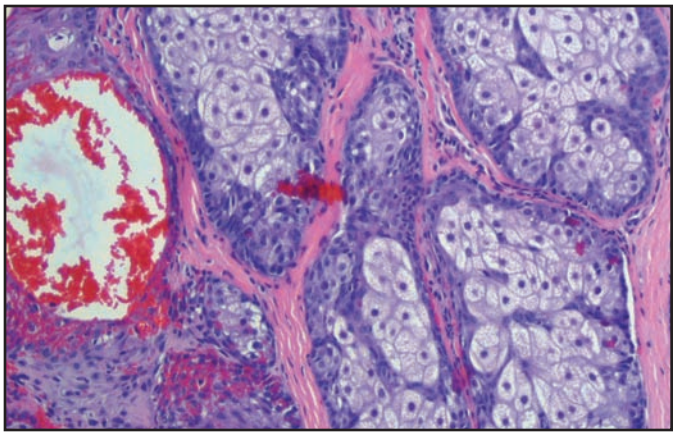

FIGURE 2. H&E, original magnification x100. Shave biopsy of the left jaw line showing numerous pyriform sebaceous lobules associated with an increased number of immature sebocytes at their periphery. The lobules are oriented perpendicularly to the skin surface.

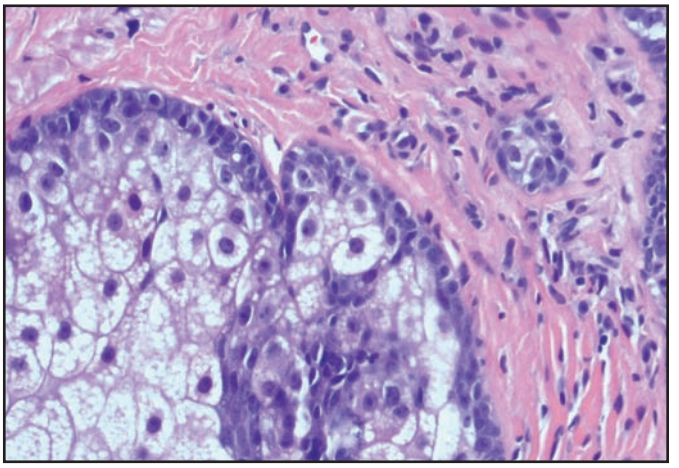

FIGURE 3. H&E, original magnification x200. Shave biopsy of sebaceous adenoma showing increased number of darker germinative cells at the periphery of the sebaceous lobules.

first clue in the diagnosis of MTS, but it is more commonly found after a visceral malignancy is diagnosed. Sebaceous neoplasms precede visceral cancer diagnosis in 22 percent of patients, occur simultaneously in six percent, and appear after in 56 percent of reported cases.[1,2,4] The mean age for appearance of cutaneous neoplasms is 53 years, and the mean age for detection of the initial visceral neoplasm is 50 years.[1,4]

MTS-associated visceral malignancies are less aggressive than their sporadic counterparts. As a result, most patients have good long-term survival even in the setting of metastatic disease.[2,4] According to Ponti et al, about 60 percent of patients with MTS will develop metastatic disease.[8]

Even though these visceral malignancies are less aggressive, they are often multiple and therefore require close follow up.[13] The following are recommendations based on Cohen et al.[14] Each year a thorough physical examination should be performed and should include breast, digital rectal, testicular, thyroid, and oral examinations. Annual laboratory studies should be performed including carcinoembryonic antigen, complete blood count, and erythrocyte sedimentation rate. Yearly chest radiography and mammography should also be performed. Every 3 to 5 years, a colonoscopy or barium enema and endometrial biopsy should be obtained.[3,14] Management of patients and their families requires a multidisciplinary approach, including a primary care physician, dermatologist, gastroenterologist, surgeon, and oncologist.[4]

CONCLUSION

MTS is a genodermatosis in which sebaceous neoplasms occur together with visceral malignancies. It is a rare cancer syndrome that requires early diagnosis, thorough screening, aggressive treatment of cutaneous and visceral tumors, and genetic counseling for patients and family members. Long-term survival rates for MTS patients are high since most tumors are responsive to treatment, even in the presence of metastatic disease.

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